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Pain-related mood influences pain perception differently in fibromyalgia and multiple sclerosis

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Abstract: In patients, the perception of pain intensity may be influenced by the subjective representation of their disease. Although both multiple sclerosis (MS) and fibromyalgia (FM) possibly include chronic pain, they seem to elicit different disease representations because of the difference in their respective etiology, the former presenting evidence of underlying lesions as opposed to the latter. Thus, we investigated whether patients with FM differed from patients with MS with respect to their perception of "own" pain as well as others' pain. In addition, the psychological concomitant factors associated with chronic pain were considered. Chronic pain patients with FM (n=13) or with MS (n=13) participated in this study. To assess specific pain-related features, they were contrasted with 12 other patients with MS but without chronic pain and 31 controls. A questionnaire describing imaginary painful situations showed that FM patients rated situations applied to themselves as less painful than did the controls. Additionally, pain intensity attributed to facial expressions was estimated as more intense in FM compared with the other groups of participants. There is good evidence that the mood and catastrophizing reactions expressed in FM differentially modulated the perception of pain according to whether it was their own pain or other's pain.

Keywords: chronic pain, self and other's perspective, imaginary pain, facial expression

Introduction

The perception of pain includes both an objective experience made of somatic sensory processes and a subjective experience consisting of affective–motivational features, as the consequence of actual or potential tissue damage (nociception). Thus, individuals base the estimation of their pain on objective sensory criteria, but also, they learn how to graduate their sensations according to personal values and beliefs. For instance, a study found that people who assessed their past and future health as poor reported more present pain.[1] Generally, the awareness of inner self is a complex and multifactorial variable, and self-assessment of one's own pain is a challenging task. People tend to make biased evaluations of themselves and to use different criteria for judging themselves and others. For instance, normal volunteers reported a much more positive opinion of themselves than of others.[2,3] In the pain domain, studies on empathy have shown that healthy participants scored pain with higher intensities when they experienced it than when they observed another individual in pain.[4] These results are consistent with the view that empathy is not a simple resonance of affect between the self and others[5] but requires a more complex perspective. These results also suggest a large influence of subjective mechanisms in the attribution of pain intensity in normal volunteers. Accordingly, pain in self and in others have shown different patterns of

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activation of the sensory discriminative areas of the brain[6,7] but shares similar neural activations in the anterior cingulate cortex and anterior insula, both are known to participate in the (subjective) affective–motivational component of pain.[8,9]

Chronic diseases without evidence of lesions in the discriminative system but with psychogenic dysfunctions may be considered as interesting models to investigate how chronic pain influences the evaluation of "own" pain and others' pain. Fibromyalgia (FM) may be considered as the prototype for these diseases, contributing to pain persistence[10,11] and showing abnormal activation in the nociceptive system, particularly, in the anterior cingulate cortex.[12,13] By contrast, multiple sclerosis (MS) is a disease that is systematically associated with lesions of the central nervous system and that is frequently associated with pain symptoms. Intuitively, it seems evident that being in chronic pain or having a chronic disease may induce more empathy towards others' pain. Additionally, it has been shown that chronic pain is accompanied by psychological symptoms, such as a propensity for catastrophizing, as well as by levels of anxiety and depression that are higher than normal.[14–16] Therefore, this paper examined the impact of chronic pain on the perception of pain by paying particular attention to the psychological factors concomitant to the chronic pain.

The present study specifically addressed whether or not the presence of chronic pain has an effect on how people estimate painful experiences in themselves and in others. The study was initiated in patients with FM and was extended to a matched population of patients with MS and chronic pain. To discriminate the respective effects of chronic pain and the disease itself, two groups of MS patients were formed according to whether they suffered from pain (the MS-P group) or not (the MS-NP group). The FM group and both groups of MS patients were matched to a group of healthy volunteers. Since FM is often accompanied by behavioral and psychological symptoms, such as a propensity for catastrophizing,[17] as well as by levels of anxiety and depression that are higher than normal,[18,11] we assumed that the levels of catastrophizing, anxiety, and depression would be higher in this group than in the MS-P group. In addition, anxiety, depression, and the "dramatization of pain" have been shown to increase the pain experience;[19] consequently, we speculated that patients with FM would have a greater tendency to overestimate pain than would the other groups. In other words, patients with FM would have more difficulty discriminating the different intensities of pain in various imaginary situations and displayed from facial expressions. Precisely, this difficulty should express itself in a higher score when they would have to imagine the intensity of pain felt in various imaginary situations, especially concerning their own pain; we further speculated that the FM group should assess painful facial expressions as more intense compared with the other group.

Methods

Participants

Thirty-eight patients and 31 healthy participants gave written informed consent, according to the Declaration of Helsinki. The sociodemographic data of the participants are presented in Table 1.

Thirteen patients with FM were referred by the Pain Unit of the Saint-Etienne Hospital, Saint-Priest-en-Jarez, France and met the diagnostic criteria for FM.[20] The mean duration of the disease was 5.07 years (standard deviation [SD]: ±3.01 years).

Twenty-five patients with MS were selected from the Department of Neurology at the Saint-Etienne University Hospital and the Germaine Revel Center at Saint-Maurice-sur-Dargoire, France. All of these patients fulfilled the inclusion criteria for MS as defined by the United States National Multiple Sclerosis Society in 1996.[21] Five patients had primary progressive MS, nine patients had relapsing remitting MS, and nine patients secondary progressive MS. They were split into the two groups MS-P and MS-NP according to whether they had pain or not in order to discriminate the respective effects of chronic pain and of the disease itself.

Pain falls into two categories: primary pain and secondary pain. For the present study, we included only MS patients with primary pain, in other words, with neuropathic pain, according to the criteria of O'Connor et al.[22] Patients, especially those in the MS group, with secondary pain, such as pain of psychological origin or pain associated with spasticity symptoms, were not included.

Table 1 Participants' characteristics

	Controls	FM	MS-P	MS-NP
Men/women	11/20	0/13	5/6	7/5
Age (range)	49 (35–65)	52.7 (37–76)	50.16 (38–65)	51.08 (36–73)
Education†	2.1 (0.83)	2.08 (0.86)	2.42 (0.79)	2.25 (0.96)
MMSE	28.45 (1.65)	27.03 (2.00)	27.78 (1)	28.75 (1.2)
MOCA	26.45 (2.88)	23.6 (3.00)*	25.5 (3.3)	25.8 (2.5)

Notes: Data represent mean (standard deviation) values. FM = the group of patients with fibromyalgia; MS-P = the group of multiple sclerosis patients with pain; MS-NP = the group of multiple sclerosis patients without pain. *Significantly differed from controls ($P<0.05$). †Education levels: 1= primary education; 2= secondary education; 3= college education.

Abbreviations: MMSE, Mini Mental State Examination; MOCA, Montreal Cognitive Assessment.

For both FM and MS patients, the exclusion criteria were as follows: other neurologic diseases, history of psychiatric illness, history of head trauma, history of alcohol or drug abuse, or present use of narcotics. Isolated mood disorder was not an exclusion criterion for these patients. All participants in the FM and MS groups had unchanged doses of medication.

Since cognitive impairments have been reported in both FM [23,24] and MS,[25] patients were tested with the Mini Mental State Examination Test (MMSE)[26,27] and the Montreal Cognitive Assessment (MOCA)[28] (Table 1).

The exclusion criteria for healthy participants included any current psychiatric or neurological disorder. None of the control participants were taking psychoactive medication. The patient and control groups showed no significant differences with respect to age and educational level (Table 1).

Materials and procedure

Mood disorders and pain catastrophizing assessment

Depressive mood and anxiety were evaluated using the Self-assessment Questionnaire of Depression (QD2A)[29] for depressive symptomatology and the Anxiety Scale Questionnaire,[30] respectively. The cutoff thresholds were ≥7 for the QD_2A and ≥5 for the Anxiety Scale Questionnaire. The French Canadian version of the Pain Catastrophizing Scale (PCS-CF)[31] was used to assess pain catastrophizing.

Situational Pain Questionnaire

The procedure and tasks used in the present study, to assess the perception of pain in FM and MS patients compared to controls, were similar to those used in the Danziger et al study.[32] Firstly, to evaluate how FM and MS patients estimate their own pain sensitivity and the pain sensitivity of others, we used the French version of the Situational Pain Questionnaire (SPQ)-30 items version.[33] This includes 15 descriptions of painful events (eg, "The dentist drilled one of your teeth without anesthesia") and 15 nonpainful events (eg, "Someone is bitten by a mosquito"). Participants completed two versions of the SPQ on the same sheet – one version interrogating their imagining of their own pain sensations in different situations (SPQ_{self}) and the second, the pain sensations they imagined in a normal other individual of the same gender and age (SPQ_{other}).

The items were evaluated using a numerical rating scale ranging from 1 (not noticeable) to 10 (worst possible pain) and yielded a discrimination score and a response bias score. The discrimination score P(A) indicates the ability of subjects to differentiate painful and painless situations. The P(A) can vary between 0 and 1: a score of 0 means no discrimination, a score of 0.5 is equivalent to a choice by chance, and a score of 1.0 represents perfect discrimination. The response bias (B) score indicates the extent to which the situations can be considered as painful. The less painful the situations are considered, the higher the B score. Both the P(A) and the B score were calculated as two scores, respectively $P(A)_{self}$ and $P(A)_{other}$, and B_{self} and B_{other}.

Faces expressing pain

Additionally, the ability of patients to estimate the intensity of the pain of others from their facial expressions was assessed using the Sensitivity to Expressions of Pain Test (STEP Test).[34] This test consists of video clips showing facial expressions of patients undergoing different active and passive movements of their shoulders, some being painful. These clips were sampled and classified according to the intensity of pain reported using the Facial Action Coding System.[35] Facial Action Coding System is a method of describing facial movements developed by psychologists Ekman and Friesen in 1978.[35]

Sixty 1-second sequences were randomly presented, with 20 depicting no pain, 20 depicting strong pain, and 20 depicting moderate pain. Three pretest sequences were used as examples before the 60 items were presented. The participants were asked to determine whether the sequence represented "no pain" (score 0), "moderate pain" (score 1), or "strong pain" (score 2). The scores were based on the nonparametric model of the signal detection theory, which provided two scores for discrimination P(A) and two scores for response bias (B): the difference between "no pain" and "moderate pain" expressions (P[A]NM and BNM); and the difference between "no pain" and "strong pain," expressions (P[A]NS and BNS). P(A) and B values were calculated in similar manner as those for the SPQ. Note here that the response bias scores of the STEP Test were computed in such a manner that the higher the response bias, the higher the pain inferred. In contrast, the analyses conducted for the SPQ let to interpret the results as follows: the less painful the situations are considered, the higher the B score.

Data analyses

For each group, the mean scores were collected from the QD2A scale, the Anxiety Scale Questionnaire, and the Pain Catastrophinzing scale. Additionally, as mentioned, the P(A) and the B scores were calculated on data collected from the SPQ and STEP tests. Considering the small number of patients, the P(A) and the B scores were each rank-transformed[36] and treated to a separate analysis of variance (ANOVA) and of covariance (ANCOVA) with the group as the between-groups factor; the depression, anxiety, and catastrophizing variables were used as covariates. Post hoc comparisons were carried out using the Bonferroni adjustment.

Results

Mood and catastrophizing assessments

As described in Table 2, all patients with chronic pain (ie, the FM and MS-P groups) showed higher depression and anxiety scores than did the controls. The patients with FM had a higher catastrophizing score than did the controls, whereas the patients with MS-P did not differ from controls. As the likelihood of anxiety, depression, and catastrophizing was increased among the FM patients, these variables were used as covariates in the later analyses.

Rating of imaginary situations (SPQ)

Firstly, the ANOVAs revealed a main effect of group ($F[3,64]=6.41$) ($P=0.0007$) for the version of the SPQ applied to the "self:" the FM patients showed a significantly lower P(A) than did the controls, $P(A)_{self}=0.76$ (standard deviation [SD]: 0.09) versus 0.88 (SD: 0.07), respectively ($P<0.0001$). This pattern of results indicates that the FM patients were less able than others to differentiate between painful and non-painful situations that applied to themselves (see Figure 1). Though ANOVA analyses revealed significant differences, no effect was revealed with the ANCOVA analyses. This means that the significant differences observed between the groups were due to the psychological factors assessed.

Similarly, ANOVAs revealed a main effect of group, $F(3,64)=3.02$ ($P=0.03$), when the B score was considered as the dependent variable. The FM patients showed significantly higher B scores than did the controls ($B_{self}=6.07$ [SD: 1.73] versus 5.04 [SD: 1.31], respectively) ($P=0.03$) or than the MS-P patients ($B_{self}=5.13$ [SD: 1.52]) ($P=0.0002$), indicating that they were less able than others to consider imaginary stimuli that applied to themselves as painful (see Figure 2). Once again, the ANCOVA analyses revealed no effect.

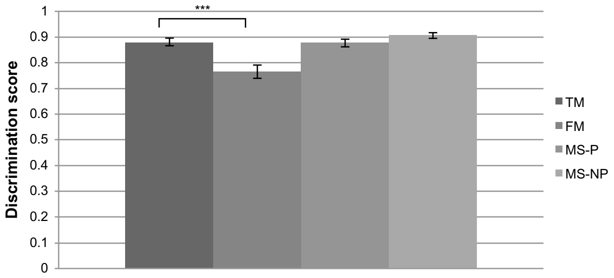

Figure 1 SPQ discrimination score for "self" pain.

Notes: Variability appears in terms of standard errors. ***Significant differences ($P<0.0001$) were reported.

Abbreviations: FM, fibromyalgia patients; MS-P, multiple sclerosis patients with pain; MS-NP, multiple sclerosis patients with no pain; SPQ, Situational Pain Questionnaire; TM, normal controls.

Table 2 Pain and mood assessments

	Controls	FM	MS-P	MS-NP
Depression scale	3.46	7.83	7.07	2.83
	(2.82)	(12.57)**	(4.09)**	(2.72)
Anxiety scale	4.3	5.28	5.84	1
	(2.49)	(1.21)**	(2.91)**	(1.04)*
PCS-CF	24.41	30	23.6	26 (7)
	(9.04)	(9.78)*	(12.05)	

Notes: Data represents mean (standard deviation) values. FM = the group of patients with fibromyalgia; MS-P = the group of multiple sclerosis patients with pain; MS-NP = the group of multiple sclerosis patients without pain. *Significantly differed from controls ($P<0.05$); **patients with pain significantly differed from controls and MS patients without pain.

Abbreviation: PCS-CF, French Canadian Pain Catastrophizing Scale.

Finally, no significant difference was observed in the ratings of the SPQ applied to others.

Facial expressions of pain (STEP test)

Differences were mainly observed in the P[A]NM score (between faces expressing "moderate pain" and those expressing "no pain") ($F[3,64]=3.09$) ($P=0.03$), and significant differences were found between the FM patients and the controls ($P=0.01$), between the MS-P patients and the controls ($P=0.03$), and with a trend toward significance between the MS-NP patients and the controls ($P=0.06$). This effect reflects that all patients, even MS-NP patients, were less able than controls to correctly distinguish subtle differences of intensity in facial expression (see Table 3).

The B score between "no pain" and "strong pain" on one hand and between "no pain" and "moderate pain" on the

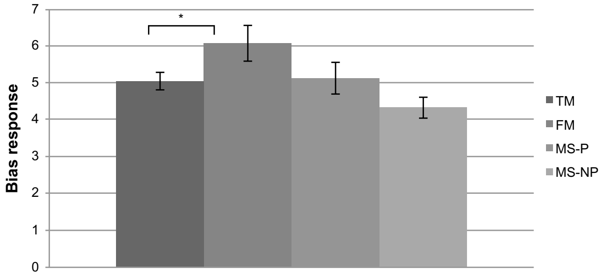

Figure 2 SPQ response bias for "self" pain.

Notes: Variability appears in terms of standard errors. *Significant differences ($P<0.05$) were reported.

Abbreviations: FM, fibromyalgia patients; MS-P, multiple sclerosis patients with pain; MS-NP, multiple sclerosis patients with no pain; SPQ, Situational Pain Questionnaire; TM, normal controls.

Table 3 Sensitivity to facial expressions of pain (STEP test)

Score	Controls	FM	MS-P	MS-NP
Discrimination scores				
P(A)NS	0.95 (0.03)	0.92 (0.02)*	0.95 (0.008)	0.90 (0.08)*
P(A)NM	0.77 (0.01)	0.70 (0.02)*	0.71 (0.01)*	0.72 (0.06)
Response bias score				
BNS	1.3 (0.05)	1.67 (0.1)*	1.46 (0.07)	1.38 (0.1)
BNM	0.94 (0.04)	1.20 (0.1)*	0.90 (0.05)	0.96 (0.06)

Notes: The discrimination score, P(A), indicates the extent to which participants were able to differentiate facial expressions. The response bias (B) score indicates patients' tendency to infer pain from the facial expressions. Two discriminations scores and two bias scores were analyzed: NS (between "no pain" and "strong pain" expressions) and NM (between "no pain" and "moderate pain" expressions). The data represent mean (errors standard) values. *Significant differences between patients and controls ($P<0.05$).

Abbreviations: FM, fibromyalgia patients; MS-P, multiple sclerosis patients with pain; MS-NP, multiple sclerosis patients with no pain.

other hand showed a main effect of group (F[3,64] =3.54 [P=0.01] and F[3,64] =2.8 [P=0.04], respectively). Only the FM patients differed from the controls ("no pain" vs "strong pain") (P=0.0009) (Table 3) and from the other groups ("no pain" vs "moderate pain") ($P<0.01$), in their manner of inferring increased pain intensities from facial expression.

When depression, anxiety, and catastrophizing were used as covariates, no significant difference was observed between the groups.

Discussion

FM patients showed significantly more mental distress, including depression and anxiety, than did the healthy controls. These findings replicate other studies showing a link between FM, anxiety and depression.[11,37] Interestingly, these abnormalities were shared with the group of patients having MS and chronic pain. In contrast, the patients with FM were the only group of patients to overdramatize their pain in comparison with the control group. Therefore, within the field of this study, catastrophizing seems specific to FM but not to chronic pain. It has been reported that pain catastrophizing is significantly correlated with increased activity in the brain areas subserving anticipation, attention, and the emotional aspects of pain,[13] suggesting possible cognitive or fearful biases towards potentially painful events. Increased catastrophizing as well as the presence of anxiety and depression in FM should have led patients to assign a higher negative value to external painful stimuli.[38] Contrary to these predictions, the FM patients imagined pain situations applied to themselves as less painful than did the other groups. This downplay in the representation of pain intensity for external events applied to themselves (as described in the SPQ, for example, pain felt at the dentist) may suggest that they considered these painful situations to be less intense than their everyday pain. Conversely, when imaging pain in others, the performance of patients with FM did not differ from the control group, suggesting an intact ability for empathy. Similar abilities to properly assess pain in others have been previously reported in the extreme clinical situation of patients who never experience pain (congenital insensitivity to pain).[32] These results suggest that it is possible to adequately describe pain intensity in others through general knowledge and semantic cues, even in the absence of previous experience,[32] and a similar explanatory mechanism may apply to patients with FM. Such a semantic process does not apply to their own pain in patients with MS, suggesting a primary reference to their own emotional or sensorimotor maps. This discrepancy seen between the normal judgment of others' pain based on semantic criteria and the downregulation of their own pain intensity processes seems relatively specific to FM patients, since it was not observed in MS-P patients.

Additionally, the patients with FM did not appear to benefit from emotional cues during the presentation of facial expressions since they overrated pain intensity as compared with controls. This result differs from findings in patients with congenital insensitivity to pain who had relatively normal performances – in spite of the absence of painful experiences, they were able to detect pain appropriately out of the emotional cues induced by facial expressions.[32] Since facial expressions are thought to involve the affective component of pain experience in the anterior cingulate cortex and the insula,[8,24] a first hypothesis could be that patients with FM have increased sensitivity in this affective field, consistent with other experimental data.[39] An alternative hypothesis could be that patients with FM show excessive empathy when evaluating facial expressions of pain because they tend to project their own pain onto the stimuli. Accordingly, patients with MS, with or without pain, were less able than controls to distinguish the different intensities of pain on faces but showed very similar B scores. As compared with FM, they had very slight and restricted abnormalities in the area of empathy. This difference between patients with MS and those with FM may be explained first by the etiology of the disease that is clearly somatic for the former and with a potent psychosomatic component for the latter.

In conclusion, our results showed that the psychological factors concomitant to pain, especially in FM, are variables that minimized the judgment of pain intensity attributed to a situation of "own" pain, as evoked by semantic cues in the FM patients. This is a quite specific pattern of response, absent in patients with chronic pain from other origins. This is a pattern of response that does not apply to judgment of pain in others, suggesting, in FM patients, a normal empathic reaction to these semantic cues. In addition, the FM patients showed an increased empathic reaction based on emotional cues, as assessed with facial expressions, suggesting a generalized enhanced sensitivity to painful events. Again, this may be a relatively specific pattern of dysfunction since it is not observed in other patients with chronic pain.

The small number of participants may constitute one of the weak points of this study; however, even with weak statistical power, the results show significant differences, highlighting the importance of considering these results. Further studies seem necessary because of the small size of the group and to more precisely test the relative contributions of discriminative, emotional, and empathic reactions in patients with FM, to specify which of these components are impaired in FM.

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Disclosure

The authors report no conflicts of interest in this work.

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